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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte MICHAEL D. DOYLE, MAURICE J. PESCITELLI JR., BETSEY S. WILLIAMS and GEORGE S. MICHAELS

Appeal 2008-005145
Application 09/916,709
Technology Center 1600

Decided:[1] June 9, 2009

Before ERIC GRIMES, RICHARD M. LEBOVITZ, and JEFFREY N. FREDMAN, *Administrative Patent Judges*.

GRIMES, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a method of combining image data and biological data from the same tissue sample.

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[1] The two-month time period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, begins to run from the decided date shown on this page of the decision. The time period does not run from the Mail Date (paper delivery) or Notification Date (electronic delivery).

The Examiner has rejected the claims as indefinite and obvious. We have jurisdiction under 35 U.S.C. § 6(b). We reverse both rejections.

STATEMENT OF THE CASE

The Specification discloses a process referred to as "spatial genomics" that fulfills "a need to correlate gene expression data with morphological structure in a useful and easy to understand manner, such as in a volume visualization environment" (Spec. 6, ¶¶ 23, 25).

The Specification describes an example of the disclosed process, in which a tissue sample is cut into histological thin sections, "producing two sets of alternating serial sections" (*id.* at 7, ¶ 33). One set of sections is used to generate image data via light microscopy (*id.*). The other set of sections is used to generate gene expression data: a "UV laser . . . is used to incise a grid pattern across each tissue section of the [second] set" and "each incised section sample from each grid location of each section . . . [is transferred] to a uniquely-coded isolation tube for lysis and further processing" for cDNA microarray analysis (*id.* at ¶¶ 35-39).

"The gene expression data . . . are then spatially mapped onto the original multidimensional morphological matrix of image data . . . [by] superimpos[ing] the expression message distribution upon the morphological volume image data" (*id.* at 8, ¶ 41).

Claims 1-4, 6, 7, and 9-11 are pending and on appeal. Claim 1 is representative and reads as follows:

> 1. A method for creating a multidimensional morphological reconstruction of biological data characterizing a biological tissue comprising the steps of:

cutting histologically thin sections of said biological tissue to produce first and second sets of alternating serial sections of said biological tissue;

mapping image data obtained from the first set of alternating serial sections onto a tissue space coordinate system to construct a multidimensional morphological tissue space matrix of image data of the first set of alternating serial sections;

unattendedly micro dissecting each serial section in the second set of alternating serial sections into a set of micro dissected section samples;

assigning a unique code to each micro dissected section sample micro dissected from the second set of alternating serial sections to form a set of coded micro dissected section samples, with each unique code indicating tissue space coordinates of each coded micro dissected section sample in the morphological tissue space matrix;

analyzing each coded micro dissected section sample to obtain biological data providing information on a plurality of biological characteristics of the coded micro dissected section sample; and

spatially mapping the biological data characterizing each coded micro dissected section sample, micro dissected from the second set of alternating serial sections, onto the multidimensional morphological tissue space matrix, constructed from the first set of alternating serial sections and superimposing the biological data of the coded micro dissected section sample upon volume image data indicated by the code assigned to the coded micro dissected section sample.

The claims stand rejected as follows:

- Claims 1-4, 6, 7, and 9-11 under 35 U.S.C. § 112, second paragraph, as indefinite (Ans. 4);

• Claims 1-3, 6, 7, and 9-11 under 35 U.S.C. § 103(a) as obvious in view of Heppelmann,[2] Cole,[3] Farr,[4] Emmert-Buck,[5] and Lemelson[6] (Ans. 5); and

• Claim 4 under 35 U.S.C. § 103(a) as obvious in view of Heppelmann, Cole, Farr, Emmert-Buck, Lemelson, and Bogen[7] (Ans. 13).

DEFINITENESS

Issue

The Examiner has rejected claims 1-4, 6, 7, and 9-11 on the basis that the phrase "unattendedly micro dissecting" is indefinite (Ans. 4). The Examiner concludes that "[i]t is unclear what Applicant means by this phrase. It is unclear by what or by whom the micro dissecting is unattended." (Ans. 4).

Appellants contend that when the claim is read in light of the Specification's paragraph 35, it is clear that "unattendedly micro dissecting" means "micro-dissection without any selection by an investigator" (Br. 5).

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[2] B. Heppelmann et al., *Serial sectioning, electron microscopy, and three-dimensional reconstruction of fine nerve fibres and other extended objects,* 156 Journal of Microscopy 163-172 (1989)
[3] Kristina A. Cole et al., *The genetics of cancer—a 3D model,* 21 Nature Genetics supplement 38-41 (1999)
[4] Farr et al., US 5,811,231, issued September 22, 1998
[5] Michael R. Emmert-Buck et al., *Laser Capture Microdissection*, 274 Science 998-1001 (1996)
[6] Lemelson, US 6,058,323, issued May 2, 2000
[7] Bogen et al., US 6,281,004 B1, issued Aug. 28, 2001

The issue with respect to this rejection is: Did the Examiner err in concluding that the phrase "unattendedly micro dissecting" makes the scope of the claims unclear?

Findings of Fact

1. The Specification states that, in laser capture microdissection, a "UV laser is . . . used to perform cold ablation of thin lines of tissue, creating an incision around a specific area of the tissue section" (Spec. 4, ¶ 16).

2. The Specification states that Cole used laser capture micro-dissection "to study the cellular-level gene expression activity associated with prostate cancer" by precisely excising "specific tumor cells within the prostate gland for microarray analysis of expression activity" (*id.* at 4, ¶ 18).

3. The Specification states that Cole's "study focused on only small groups of specific tissue areas, since the microdissection approach requires a skilled operator and is extremely exacting work" (*id.*).

4. In describing an example of the disclosed method, the Specification states that a "UV laser of the type described in Cole . . . is used to incise a grid pattern across each tissue section of . . . [one] set of alternating sections. . . . This is done with the use of said UV laser adapted to the application end of a microarray-creation robotic apparatus." (*Id.* at 7-8, ¶ 35.)

5. The Specification states that incising a grid pattern using a laser adapted for use by a robotic apparatus "allows for unattended section incising of a large number of specimens" (*id.*).

Principles of Law

"The test for definiteness is whether one skilled in the art would understand the bounds of the claim when read in light of the specification." *Miles Laboratories Inc. v. Shandon Inc.*, 997 F.2d 870, 875 (Fed. Cir. 1993).

"A decision on whether a claim is invalid under § 112, 2d ¶, requires a determination of whether those skilled in the art would understand what is claimed when the claim is read in light of the specification." *Orthokinetics Inc. v. Safety Travel Chairs Inc.*, 806 F.2d 1565, 1576 (Fed. Cir. 1986).

Analysis

The Specification states that a prior art study using laser capture microdissection to precisely excise tumor cells from prostate tissue focused on specific tissue areas because that approach requires a skilled operator. The Specification also states that the same type of laser can be adapted to a robotic apparatus and used to incise a grid pattern across a set of tissue sections, and that the robotically operated laser allows for "unattended section incising" of the tissue specimens.

In our view, when the claim language is viewed in light of the Specification, it is clear that "unattendedly microdissecting" is intended to distinguish the microdissecting step in the claimed process from a process like that of Cole, where a human operator actively controls the movement of a laser as it is microdissecting a sample.

The Specification provides an example of unattended microdissection: a robotic apparatus programmed to move a laser across a sample in a grid pattern. The claimed process is, of course, not limited to the example provided in the Specification, but the example informs the analysis of what

the claim means by "unattendedly micro dissecting." Read in light of the Specification, "unattendedly micro dissecting" would be understood to mean microdissection carried out without real-time control by a human operator of the microdissection pattern.

Conclusion of Law

The Examiner erred in concluding that the phrase "unattendedly micro dissecting" makes the scope of the claims unclear.

OBVIOUSNESS

Issue

The Examiner has rejected claims 1-3, 6, 7, and 9-11 under 35 U.S.C. § 103(a) as obvious in view of Heppelmann, Cole, Farr, Emmert-Buck, and Lemelson (Ans. 5). The Examiner finds that the limitation of "unattendedly micro dissecting," as recited in each of the independent claims on appeal, is disclosed by Emmert-Buck, which "describe[s] automatic microdissection without manual procedure and a laser applied to specific locations of the film to procure specifically targeted cells that can then be transferred" (*id.* at 9).

The Examiner finds that the other limitations of the claimed method are taught by the other references (*id.* at 5-10), and concludes that the claimed method as a whole would have been obvious in view of the combined teachings of the references (*id.* at 10-13).

Appellants contend that none of the references disclose some of the claim limitations, including "unattendedly micro dissecting each serial sample into a set of micro dissected section samples" (Br. 8).

The issue with respect to this rejection is: Did the Examiner err in concluding that the cited references taught or would have suggested the claimed method, including the step of unattendedly micro dissecting each section in a set of alternating serial sections?

Additional Findings of Fact

6. The Examiner finds that "Heppelmann et al. do not describe unattendedly microdissecting" (Ans. 6).

7. The Examiner finds that "Cole et al. do not teach unattendedly microdissecting" (*id.* at 8).

8. The Examiner finds that "Farr et al. do not teach unattendedly microdissecting" (*id.* at 9).

9. The Examiner finds that "Emmert-Buck et al. describe automatic microdissection without manual procedure and a laser applied to specific locations of the film to procure specifically targeted cells that can then be transferred (page 998, third column, first full paragraph and abstract, lines 5-9) which represents unattendedly microdissecting" (*id.*).

10. The Examiner does not rely on Lemelson for any disclosure of unattended microdissection (*id.* at 9-10).

11. Emmert-Buck discloses that "[s]everal methods have been reported for tissue microdissection to address the problems associated with analysis of heterogeneous tissue. These include gross dissection from frozen tissue blocks . . . and microdissection with manual tools" (Emmert-Buck 998, middle col.).

12. Emmert-Buck states that "although manual microdissection can achieve good precision, it is time-consuming, labor-intensive, and requires a high degree of manual dexterity" (*id.*).

13. The abstract of Emmert-Buck reads as follows:

> Laser capture microdissection (LCM) under direct microscopic visualization permits rapid one-step procurement of selected human cell populations from a section of complex, heterogeneous tissue. In this technique, a transparent thermoplastic film (ethylene vinyl acetate polymer [EVA]) is applied to the surface of the tissue section on a standard glass histopathology slide; a carbon dioxide laser pulse then specifically activates the film above the cells of interest. Strong focal adhesion allows selective procurement of the targeted cells. Multiple examples of LCM transfer and tissue analysis, including polymerase chain reaction amplification of DNA and RNA, and enzyme recovery from transferred tissue are demonstrated.

(*Id.* at 998.)

14. Emmert-Buck discloses that "LCM has several advantages over current tissue microdissection approaches: It is simple, requires no moving parts, involves no manual microdissection or manipulations, and enables one-step transfers" (*id.* at 998, right col., first full paragraph).

15. Emmert-Buck discloses that, in LCM, a "[t]ransparent EVA thermoplastic film is applied to the surface of a routine tissue section mounted on a glass slide. The tissue-EVA film sandwich is viewed under a microscope, and the cells of interest are positioned in the center of the field." (*Id.* at 998, legend to Fig. 1A.)

16. Emmert-Buck discloses that "a single region of tissue can be transferred to the film, or alternatively, the operator may move the slide and transfer multiple regions to the same film" (*id.* at 999, left col.).

17. Emmert-Buck discloses that "an individual glomerulus can be completely procured from a kidney tissue section in <10 s, and hundreds of glomeruli can be procured by an individual LCM operator in 1 hour with minimal effort" (*id.* at 999, left col. to middle col.).

18. Emmert-Buck discloses that "the LCM operator visualizes the transfer and can thus verify the specificity of the procured material" (*id.* at 999, middle col.).

Principles of Law

"The test of obviousness *vel non* is statutory. It requires that one compare the claim's 'subject matter as a whole' with the prior art 'to which said subject matter pertains.'" *In re Ochiai*, 71 F.3d 1565, 1569 (Fed. Cir. 1995) (quoting 35 U.S.C. § 103).

A proper § 103 analysis requires "a searching comparison of the claimed invention – including all its limitations – with the teaching of the prior art." *Id.* at 1572.

"In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a *prima facie* case of obviousness." *In re Rijckaert*, 9 F.3d 1531, 1532 (Fed. Cir. 1993).

Analysis

The Examiner relies on Emmert-Buck for disclosure of the step of "unattendedly micro dissecting" serial sections of a tissue sample. Emmert-Buck, however, makes clear that the LCM method relies on an operator to select specific regions of a tissue section for procurement. See FFs 15-18. Emmert-Buck's statement that LCM "involves no manual microdissection"

(FF 14) is not to the contrary. It is clear from the context that Emmert-Buck's reference to "manual microdissection" means the previously reported technique of "microdissection with manual tools" (FF 11), which had the drawbacks that it was "time-consuming, labor-intensive, and require[d] a high degree of manual dexterity" (FF 12).

Emmert-Buck does not disclose "unattendedly micro dissecting" a tissue section and the Examiner has pointed to nothing in any of the other references to make up for that deficiency. The Examiner therefore has not established that the claimed method would have been prima facie obvious based on the cited references.

The Examiner also rejected claim 4 under 35 U.S.C. § 103(a) based on Heppelmann, Cole, Farr, Emmert-Buck, and Lemelson, further combined with Bogen (Ans. 13). The Examiner cited Bogen, however, only for the "coded tissue section sample holder, as stated in claim 4" (*id.* at 14). Claim 4 also includes the limitation of "unattendedly micro dissecting" a tissue section. For the same reason discussed above, the Examiner has not established that the method of claim 4 would have been prima facie obvious based on the cited references.

Conclusion of Law

The Examiner erred in concluding that the cited references taught or would have suggested the claimed method, including the step of unattendedly micro dissecting each section in a set of alternating serial sections.

SUMMARY

We reverse the rejections of claims 1-4, 6, 7, and 9-11 under 35 U.S.C. § 112, second paragraph, and under 35 U.S.C. § 103(a).

REVERSED

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